

In re of: 10/580,542  
Amd. dated July 22, 2009  
Reply to Office Action of January 22, 2009

**AMENDMENTS TO THE CLAIMS:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:**

**1-20. (Cancelled)**

**21. (Currently Amended)** A method of treating an immune disorder, said method comprising administering to an individual having the immune disorder a therapeutically effective amount of an agent capable of increasing or decreasing NF- $\kappa$ B inducing kinase (NIK)-SIVA ~~NIK-SIVA~~ complex formation, thereby treating the immune disorder in the individual.

**22. (Currently Amended)** The method according to claim 21, wherein said immune disorder is characterized by abnormal function or level of at least one protein selected from the group consisting of B lymphocyte stimulator protein (BLyS) ~~BLyS~~/BAFF, CD27, SIVA and NIK.

**23. (Original)** The method according to claim 21, wherein said immune disorder is selected from the group consisting of multiple myeloma (MM), acquired immunodeficiency syndrome (AIDs), Sjogren's syndrome (SS), B-cells chronic

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lymphocytic leukemia (B-CLL), systemic lupus erythematosus, inflammatory colon disease, systemic inflammatory response syndrome (SIRS), multiple organ disinfection syndrome (MODS) and acute respiratory distress syndrome (ARDS).

**24. (Original)** The method according to claim 21, wherein said administering is effected by expressing said agent within cells of said individual.

**25. (Original)** The method according to claim 24, wherein said cells of said individual are lymphocyte cells.

**26. (Withdrawn)** A method of treating an immune disorder comprising administering to an individual having the immune disorder a therapeutically effective amount of an agent capable of increasing or decreasing NIK-dependent CD27 regulation, thereby treating the immune disorder in the individual.

**27. (Withdrawn)** The method according to claim 26, wherein said administering is effected by expressing said agent within cells of said individual.

**28. (Withdrawn)** The method according to claim 27, wherein said cells of said individual are lymphocyte cells.

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**29. (Withdrawn)** A method of treating an immune disorder caused or aggravated by abnormal NF- $\kappa$ B activation via the canonical pathway, comprising administering to an individual suffering from the disorder a therapeutically effective amount of an agent capable of decreasing or increasing the activity of NIK.

**30. (Withdrawn)** A method of treating according to claim 29, wherein the agent is capable of decreasing the activity of NIK.

**31. (Withdrawn)** A method of treating according to claim 29, wherein abnormal NF- $\kappa$ B activation is caused by induction of CD40L and/or activation of the receptor thereof.

**32. (Withdrawn)** A method of treating according to claim 29, wherein abnormal NF- $\kappa$ B activation is caused by induction of CD70 and/or activation of the receptor thereof.

**33. (Withdrawn)** A method of treating according to claim 29, wherein abnormal NF- $\kappa$ B activation is caused by induction of Blys and/or activation of the receptor thereof.

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**34. (Withdrawn)** A method of treating according to claim 30, wherein the agent is an antibody.

**35. (Withdrawn)** A method of treating according to claim 34, wherein the agent is an antibody directed against the phosphorylated NIK activation loop.

**36. (Withdrawn)** A method according to claim 30, wherein the agent is a small interfering RNA molecule.

**37. (Withdrawn)** A method according to claim 36, wherein the small interfering RNA molecule is that of SEQ ID NO: 15.

**38. (Withdrawn)** A method according to claim 30, wherein the agent is a rybozyme.

**39. (Withdrawn)** An isolated polynucleotide comprising a nucleic acid sequence capable of specifically down-regulating NIK expression in cells provided thereto.

**40. (Withdrawn)** The isolated polynucleotide of claim 39, wherein the isolated polynucleotide is a small interfering RNA molecule.

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**41. (Withdrawn)** The isolated polynucleotide of claim 40, wherein said small interfering RNA molecule is that of SEQ ID NO:15.

**42. (Withdrawn)** A nucleic acid construct comprising the isolated polynucleotide of claim 39.

**43. (Withdrawn)** A cell comprising the nucleic acid construct of claim 42.

**44. (Withdrawn)** An antibody or antibody fragment capable of specifically binding to an amino acid sequence region set forth by coordinates 624-947 of SEQ ID NO:2.

**45. (Withdrawn)** An antibody or antibody fragment capable of specifically binding to an amino acid sequence region set forth by coordinates 123-175 of SEQ ID NO:3.

**46. (Withdrawn)** An antibody or antibody fragment capable of specifically binding to an amino acid sequence region set forth by coordinates 58-110 of SEQ ID NO:4

**47. (Withdrawn)** A method of identifying a putative immune modulator, the method comprising identifying a molecule

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capable of increasing or decreasing NIK-SIVA complex formation, said molecule being the putative immune modulator.

**48. (Withdrawn)** A method of identifying a putative immune modulator, the method comprising identifying a molecule capable of increasing or decreasing NIK-dependent CD27 regulation, said molecule being the putative immune modulator.

**49. (Withdrawn)** A method for the screening of molecules capable of modulating the activity of NIK comprising contacting a cell with a ligand of a TNF/NGF receptor family capable to induce NIK-dependent canonical and alternative pathway in the cell, incubating the cell prior to, after, or during said contacting with individual tested molecules, detecting activation of the canonical pathway in the cell and selecting individual molecule/s capable of modulating induction of the canonical pathway induced by said ligand.

**50. (Withdrawn)** The method according to claim 49, wherein the ligand of a TNF/NGF is selected from CD70, CD40L, and Blys/BAFF.

**51. (Withdrawn)** The method according to claim 50, wherein the cells are of a lymphoblastoid type.

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**52. (Withdrawn)** The method according to claim 51, wherein the cell is selected from Ramos, Raji and BJAB cells.

**53. (Withdrawn)** The method according to Claim 49, wherein activation of the canonical pathway is detected by monitoring parameters indicative of the canonical pathway activation, selected from I $\kappa$ B degradation, I $\kappa$ B $\alpha$  phosphorylation and p65 translocation.

**54. (Withdrawn)** A method for the screening of molecules capable of modulating NIK activity comprising contacting a lymphoblastoid cell with a ligand of a TNF/NGF receptor family capable of activating NIK and the canonical pathway in the cell, incubating the cell prior to, after, or during said contacting, with individual tested molecules, detecting activation of the canonical pathway and, selecting individual molecule/s capable of modulating induction of the canonical pathway induced by said ligand but not by any other ligand capable of inducing canonical pathway in a NIK independent manner.

**55. (Withdrawn)** The method according to claim 54, wherein the ligand of a TNF/NGF is selected from CD70, CD40L, and Blys/BAFF.

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**56. (Withdrawn)** The method according to claim 54, wherein the ligand capable of inducing the canonical pathway in a NIK independent form is TNF.

**57. (Withdrawn)** The method according to claim 54, wherein activation of the canonical pathway is detected monitoring parameters indicative of the canonical pathway activation, selected from I $\kappa$ B degradation, I $\kappa$ B $\alpha$  phosphorylation and p65 translocation.

**58. (Withdrawn)** The method according to claim 54, wherein the cell is selected from Ramos, Raji and BJAB cells.

**59. (Cancelled)**